CLAIMS

1. An antibody molecule having specificity for human TNFα, comprising a heavy chain wherein the variable domain comprises a complementarity determining region (CDR) having the sequence given as H1 in Figure 3 (SEQ ID NO:1) for CDRH1, as H2' in Figure 3 (SEQ ID NO:2) or as H2 in Figure 3 (SEQ ID NO:7) for CDRH2 or as H3 in Figure 3 (SEQ ID NO:3) for CDRH3.

2. An antibody molecule having specificity for human TNFα, comprising a light chain wherein the variable domain comprises a CDR having the sequence given as L1 in Figure 3 (SEQ ID NO:4) for CDRL1, as L2 in Figure 3 (SEQ ID NO:5) for CDRL2 or as L3 in Figure 3 (SEQ ID NO:6) for CDRL3.

3. An antibody molecule having specificity for human TNFα, comprising a heavy chain wherein the variable domain comprises a CDR having the sequence given in SEQ ID NO:1 for CDRH1, SEQ ID NO:2 or SEQ ID NO:7, for CDRH2 or SEQ ID NO:3 for CDRH3 and a light chain wherein the variable domain comprises a CDR having the sequence given in SEQ ID NO:4 for CDRL1, SEQ ID NO:5 for CDRL2 or SEQ ID NO:6 for CDRL3.

4. The antibody molecule of claim 3, which comprises SEQ ID NO:1 for CDRH1, SEQ ID NO: 2 or SEQ ID NO:7 for CDRH2, SEQ ID NO:3 for CDRH3, SEQ ID NO:4 for CDRL1, SEQ ID NO:5 for CDRL2 and SEQ ID NO:6 for CDRL3.

5. The antibody molecule of any one of claims 1 to 3, which comprises SEQ ID NO:2 for CDRH2.

6. The antibody molecule of any one of claims 1 to 3, which is a CDR-grafted antibody molecule.

7. The antibody molecule of claim 6, wherein the variable domain comprises human acceptor framework regions and non-human donor CDRs.

8. The antibody molecule of claim 7, wherein the human acceptor framework regions of the variable domain of the heavy chain are based on a human group 1 consensus sequence and comprise non-human donor residues at positions 28, 69 and 71.

9. The antibody molecule of claim 7, wherein the human acceptor framework regions of the variable domain of the heavy chain are based on a human group 1 consensus sequence and comprise non-human donor residues at positions 28, 38, 46, 67, 69 and 71.

10. The antibody molecule of claim 7, wherein the human acceptor framework regions of the variable domain of the heavy chain are based on a human group 3 consensus sequence and comprise non-human donor residues at positions 27, 28, 30, 48 49, 69, 71, 73 76 and 78.

11. The antibody molecule of claim 7, wherein the human acceptor framework regions of the variable domain of the light chain are based on human group 1 consensus sequence and comprise non-human donor residues at positions 46 and 60.

12. The antibody molecule of claim 3, comprising the light chain variable region hTNF40-gL1 (SEQ ID NO:8) and the heavy chain variable region gh3hTNF40.4 (SEQ ID NO:11).

13. The antibody molecule of any one of claims 1 to 3 which is a Fab fragment.

14. The antibody molecule of claim 13, which is a Fab fragment comprising a heavy chain having the sequence given in SEQ ID NO:111 and a light chain having the sequence given in SEQ ID NO:113.

15. The antibody molecule of claim 1, which is a modified Fab fragment having at the C-terminal end of its heavy chain one or more amino acids to allow attachment of an effector or reporter molecule.

16. The antibody molecule of claim 15, wherein the additional amino acids form a modified hinge region containing one or two cysteine residues to which the effector or reporter molecule may be attached.

17. The antibody molecule of claim 12, which is a modified Fab fragment comprising a heavy chain having the sequence given in SEQ ID NO:115 and a light chain having the sequence given in SEQ ID NO:113.

18. An antibody molecule having specificity for human TNFα, having a light chain comprising the sequence given in SEQ ID NO:113.

19. An antibody molecule having specificity for human TNFα, having a light chain consisting of the sequence given in SEQ ID NO:113.

20. An antibody molecule having specificity for human TNFα, having a heavy chain comprising the sequence given in SEQ ID NO:115.

21. An antibody molecule having specificity for human TNFα, having a heavy chain consisting of the sequence given in SEQ ID NO:115.

22. An antibody molecule having specificity for human TNFα, having a light chain comprising the sequence given in SEQ ID NO:113 and a heavy chain comprising the sequence given in SEQ ID NO:115.

23. An antibody molecule having specificity for human TNFα, having a light chain consisting of the sequence given in SEQ ID NO:113 and a heavy chain consisting of the sequence given in SEQ ID NO:115.

24. A variant of the antibody molecule of claims 1 or 2, which has an improved affinity for TNFα.

25. The variant of claim 24 which is obtained by an affinity maturation protocol.

26.. The antibody of claim 3 which is murine anti-TNFα monoclonal antibody hTNF40.

27. The antibody molecule of claim 3, which is a chimeric antibody molecule comprising the light and heavy chain variable domains of the monoclonal antibody of claim 26.

28. A compound comprising the antibody molecule claim 15 having covalently attached to an amino acid at or towards the C-terminal end of its heavy chain an effector or reporter molecule.

29. The compound of claim 28, which comprises an effector molecule.

30. The compound of claim 29, wherein the effector molecule comprises one or more polymers.

31. The compound of claim 30, wherein the one or more polymers is/are an optionally substituted straight or branched chain polyalkylene, polyalkenylene or polyoxyalkylene polymer or a branched or unbranched polysaccharide.

32. The compound of claim 31, wherein the one or more polymers is/are a methoxypoly(ethyleneglycol).

33. A compound comprising the antibody molecule of claim 17 having attached to one of the cysteine residues at the C-terminal end of the heavy chain a lysyl-maleimide group wherein each amino group of the lysyl residue has covalently

linked to it a methoxypoly(ethyleneglycol) residue having a molecular weight of about 20,000 Da.

34. A compound comprising an antibody molecule having specificity for human TNFα, having a light chain comprising the sequence given in SEQ ID NO:113 and a heavy chain comprising the sequence given in SEQ ID NO:115, having attached to one of the cysteine residues at the C-terminal end of the heavy chain one or more synthetic or naturally-occurring polymers.

35. A compound comprising an antibody molecule having specificity for human TNFα, having a light chain consisting of the sequence given in SEQ ID NO:113 and a heavy chain consisting of the sequence given in SEQ ID NO:115, having attached to one of the cysteine residues at the C-terminal end of the heavy chain one or more synthetic or naturally-occurring polymers.

36. A compound comprising an antibody molecule having specificity for human TNFα, having a light chain comprising the sequence given in SEQ ID NO:113, having attached to one of the cysteine residues at the C-terminal end of the heavy chain a lysyl-maleimide group wherein each amino group of the lysyl residue has covalently linked to it a methoxypoly(ethyleneglycol) residue having a molecular weight of about 20,000 Da..

37. A compound comprising an antibody molecule having specificity for human TNFα, having a light chain consisting of the sequence given in SEQ ID NO:113, having attached to one of the cysteine residues at the C-terminal end of the heavy chain a lysyl-maleimide group wherein each amino group of the lysyl residue has covalently linked to it a methoxypoly(ethyleneglycol) residue having a molecular weight of about 20,000 Da.

38. A compound comprising an antibody molecule having specificity for human TNFα, having a heavy chain comprising the sequence given in SEQ ID NO:115,

having attached to one of the cysteine residues at the C-terminal end of the heavy chain a lysyl-maleimide group wherein each amino group of the lysyl residue has covalently linked to it a methoxypoly(ethyleneglycol) residue having a molecular weight of about 20,000 Da.

39. A compound comprising an antibody molecule having specificity for human TNFα, having a heavy chain consisting of the sequence given in SEQ ID NO:115, having attached to one of the cysteine residues at the C-terminal end of the heavy chain a lysyl-maleimide group wherein each amino group of the lysyl residue has covalently linked to it a methoxy poly(ethyleneglycol) residue having a molecular weight of about 20,000 Da.

40. A compound comprising an antibody molecule having specificity for human TNFα, having a light chain comprising the sequence given in SEQ ID NO:113 and a heavy chain comprising the sequence given in SEQ ID NO:115, having attached to one of the cysteine residues at the C-terminal end of the heavy chain a lysyl-maleimide group wherein each amino group of the lysyl residue has covalently linked to it a methoxypoly(ethyleneglycol) residue having a molecular weight of about 20,000 Da.

41. A compound comprising an antibody molecule having specificity for human TNFα, having a light chain consisting of the sequence given in SEQ ID NO:113 and a heavy chain consisting of the sequence given in SEQ ID NO:115, having attached to one of the cysteine residues at the C-terminal end of the heavy chain a lysyl-maleimide group wherein each amino group of the lysyl residue has covalently linked to it a methoxypoly(ethyleneglycol) residue having a molecular weight of about 20,000 Da.

42. An antibody molecule comprising a hybrid CDR comprising a truncated donor CDR sequence wherein the missing portion of the donor CDR is replaced by a different sequence and forms a functional CDR.

43. The antibody molecule of claim 42, wherein the missing part of the CDR sequence is from the antibody from which the framework regions of the antibody molecule are derived.

44. The antibody molecule of claim 43, wherein the missing part of the CDR sequence is derived from a germline antibody having consensus framework regions.

45. The antibody molecule of claim 42, wherein CDRH2 of the heavy chain is hybrid in the antibody molecule.

46. The antibody molecule of claim 42, wherein the truncation of the donor CDR is from 1 to 8 amino acids.

47. The antibody molecule of claim 46, wherein the truncation is from 4 to 6 amino acids.

48. The antibody molecule of claim 42, wherein the truncation is made at the C-terminus of the CDR.

49. A DNA sequence which encodes the heavy and/or light chain of the antibody molecule of claims 3 or 42.

50. The DNA sequence of claim 49 comprising the sequence shown in SEQ ID NO:8 or 10.

51. The DNA sequence of claim 49 comprising the sequence shown in SEQ ID NO:10 or 11.

52. The DNA sequence of claim 49 comprising the sequence shown in SEQ ID NO:110, 112 or 114.

53. A cloning or expression vector containing the DNA sequence of claim 49.

54. An *E. coli* expression vector comprising the DNA sequence of claim 49.

55. The *E. coli* expression vector of claim 54 which is pTTO(CDP870).

56. A host cell transformed with the vector of claim 53.

57. A process for the production of an antibody molecule having specificity for TNFα, comprising culturing the host cell of claim 56 and isolating the antibody molecule.

58. A process for the production of an antibody molecule having specificity for TNFα, comprising culturing *E. coli* comprising an *E. coli* expression vector comprising the DNA sequence of claim 53 and isolating the antibody molecule.

59. The process of claim 58 wherein the antibody molecule is targeted to the periplasm.

60. A therapeutic or diagnostic composition comprising the antibody molecule of any one of claims 1 to 3 and 42 or the compound of claim 28.

61. A method to treat a subject with a pathology mediated by TNFα, comprising administering to the subject a therapeutically effective amount of the antibody molecule of claims 1-3 or 42, or the compound of claim 28.

62. The method of claim 68, wherein the pathology is rheumatoid- or osteo- arthritis.

63. A method to make a pharmaceutical composition for the treatment of a pathology mediated by TNFα, comprising the combining the antibody molecule of claims 1-3 or 42, or the compound of claim 28 with a pharmaceutically acceptable carrier.

64. A method to make a pharmaceutical composition for the treatment of rheumatoid- or osteo- arthritis, comprising the combining the antibody molecule of claims 1-3 or 42, or the compound of claim 28 with a pharmaceutically acceptable carrier.

65. The vector pDNAbEng-G1 as shown in Figure 19.

66. The vector pTTO(CDP870) as shown in Figure 22.

67. A polypeptide having the amino acid sequence given in any one of SEQ ID NOS:1 to 7.